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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/766,396	Applicant(s) Sutcliffe et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 8, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-44* is/are pending in the application.

4a) Of the above, claim(s) *29-44* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-28* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *21-44* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group IVa (new claims 21-28) in Paper No. 13 is acknowledged. The traversal is on the ground(s) that "all three groups should be found allowable without further search since each is claiming an antibody to a polypeptide already found allowable in parent application, U.S.S.N. 08/857,389, now U.S. Patent No. 6,479,642 B1". However, this is not found persuasive because the search and examination for polypeptides is not the same for antibodies, where only 6 amino acids are required to define an epitope that can be used to generate an antibody to a given polypeptide. Moreover, each of these polypeptide sequences are unique, which alternatively require their own search for similar sequences/ epitopes, and/or search for cross-reacting antibodies within the art. Thus, the non-coextensiveness of the search and examination for each group based on their different sequences/ epitopes would constitute an undue burden on the examiner to search and consider all the separable groups with their recognized divergent subject matter, as illustrated by the unique SEQ ID NOs of the polypeptides required to generate the claimed antibodies. The requirement is still deemed proper and is therefore made FINAL.

Claims 29-44 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 13.

Claim Rejections - 35 U.S.C. § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21-22 & 24 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "an antibody" encompasses all naturally occurring antibodies, and Fab, Fab', F(ab')2 and F(v) fragments thereof to naturally-occurring cortistatin polypeptides; thereby, not involving the hand of man to isolate or purify the antibodies, or fragments thereof. It is suggested that amending the claims to "an isolated and purified antibody ..." should obviate this rejection.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for various types of antibodies directed against specific epitopes within the cortistatin protein molecule of SEQ ID NOs. 23, 24 or 26, does not reasonably provide enablement for antibodies directed to structurally and functionally uncharacterized proteins that are merely "at least about 95% amino acid residues similar" to a SEQ ID NO when no assayable

and distinguishable functional characteristics and/or epitopes are defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification describes the human cortistatin polypeptides of SEQ ID NOS: 23, 24 & 26. Page 122 discloses that anti-cortistatin antibodies can be used to "facilitate the therapeutic amelioration of a sleep disorder, such as narcolepsy" (i.e, as it relates to the pharmaceutical compositions of claim 28). However, the name, "cortistatin" polypeptides (i.e., as defined on pages 28-30 of the specification) that are "at least about 95% amino acid residue similarity", etc., encompass any random "analog, fragment, chemical derivative..., various changes, substitutions, insertions and deletions", which sets for little structural and functional characteristics. In contrast, no functional epitope fragments nor functional epitopes from a polypeptide "having at least about 95% amino acid residue similarity to SEQ ID NO: 23, 24 and 26" are disclosed within the specification. In fact, the specification fails to teach what amino acid residues constitute a single functional cortistatin-specific epitope, or what epitopes distinguish a cortistatin-specific epitope from any different cortistatin-related protein molecule that possesses none of the desired functions of the instant invention. In other words, generation of any such antibodies, or "immunologically active fragment" thereof, without further recited and definable structural and assayable functional characteristics would be expected by the skilled artisan to result in antibodies that no longer bind to the cortistatin polypeptides of SEQ ID NOs: 23, 24 & 26, or alternatively cross-react with different proteins. For example, Geysen et al. teach that

random amino acid changes to a tetrameric peptide/epitope, which includes conservative substitutions to the same antigen, have "frequently been associated with loss of antibody binding" (e.g., pg. 38, 1st col., 2nd *pp*). Thus, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any specific cortistatin antibody binding reaction would prevent the skilled artisan from determining whether any random modification or truncation to the human cortistatin protein sequences depicted as SEQ ID NOs: 23, 24 or 26 could be made that successfully generate the desired antibodies/active fragments thereof the instant invention, because any random modification/ truncation manifested within a cortistatin protein itself would be predicted to adversely alter its biologically active 3-dimensional conformation, and therefore, the antigenic/binding site itself, without requiring undue experimentation to determine otherwise.

Second, because the specification provides little guidance as to what constitutes the metes and bounds of an otherwise open-ended and undefinable "cortistatin-like activity" (i.e., as it relates to claim 21), or for when "the antibody is *substantially* free from immunoreaction with neuropeptides other than [a structurally undefined] cortistatin" (i.e., as it relates to claim 22), one of ordinary skill in the art would not reasonably know how to make and use such antibodies or "immunologically active fragments" thereof, without requiring undue experimentation to determine such, because no distinguishable assayable functional language for the "at least about 95% amino acid residue similarity" molecules is required within the claims nor specially defined within the specification.

4. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is indefinite for when an "antibody is substantially free from immunoreaction with neuropeptides other than cortistatin", versus when an antibody is no longer "substantially free from immunoreaction...". In other words, the term "substantially free" in claim 22 is a relative term which renders the claim indefinite. The term "substantially free from immunoreaction" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

5. Claims 21-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous exactly what the recitation "at least about" entails, because "about" reasonably refers to a range of +/- 5%, whereas, the recitation "at least" removes the lower limit of the claimed range of "about 95%"; thereby, being contradictory (i.e., as it relates to claim 21).

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
July 17, 2003
Part 5/6